

CLAIMS:

1. An apparatus to provide separation and detection of components within a sample, the apparatus comprising a first separation means, an interface means, and a second separation means wherein the interface means links the first separation means and second separate means and a detector for detecting components subjected to the apparatus.

2. An apparatus of claim 1, which includes a first high voltage power source connected across the first separation means and a second high voltage power source connected across the second separation means.

3. An apparatus as claimed in claim 2, wherein said first separation means is a capillary electrophoresis system and said second separation means is a sieving electrophoresis system.

4. An apparatus for providing high sensitivity detection of components of biological samples, the apparatus comprising: a first and second separation means, each selected from the group consisting of: isoelectric focusing electrophoresis systems, SDS polyacrylamide gel electrophoresis system, a free solution electrophoresis system, a micellar electrokinetic chromatography system, a reversed phase liquid chromatography system, a normal phase chromatography system, an ion exchange chromatography system, and a size exclusion chromatography system; an interface chamber in which components separated according to said first means are mixed with a derivatizing agent prior to subjection to said second separation means; one of a first power supply and a first pump to perform the first separation means, and one of a second pump and a second power supply to perform the second separation means; and a detector.

5. The apparatus of claim 4, wherein said detector is a high sensitivity laser induced fluorescent detector.

6. The apparatus of claim 5, wherein said first separation means is an isoelectric focusing electrophoresis system, and said second separation means is a sieving electrophoresis system.

5 7. An apparatus as claimed in any preceding claim, which includes a plurality of first separation means, a plurality of second separation means, and a manifold providing a plurality of interface regions, each interface region providing an interface between a respective one of the first separation means and a respective one of the second separation means.

10 8. An apparatus as claimed in claim 7 wherein the manifold comprises an inlet, for connection to buffer reservoirs and valve means permitting selective connection to a desired buffer reservoir; a channel network connecting the inlet to the plurality of interface regions, wherein each interface region comprises a port for connection to a respective one of the first separation means, a port for connection to a respective one of the second separation means and a third, waste port.

15 9. An apparatus as claimed in claims 7 or 8, which includes a two-dimensional sheath flow cuvette, wherein the second separation means includes a plurality of capillaries, mounted in a two-dimensional array in the two-dimensional sheath flow cuvette; a light source; an optical system for illuminating ends of the capillary tubes with radiation from the light source; and an optical collection system aligned with the ends of the capillary tubes, for collecting radiation and, the optical collection system 20 optionally including a camera lens, a bandpass filter, a prism and a camera and being aligned axially with the ends of the capillary tubes.

25 10. A method of separating and detecting components in a

sample, the method comprising subjecting said sample to an apparatus which consists of high resolution separation and high sensitivity detection of components within a sample, the apparatus comprising a first separation means, an interface means, a second separation means and a detector for detecting components subjected to the apparatus, wherein the interface means links the first separation means and the second separation means, the method comprising passing the biological sample through the first separation means to achieve a first separation, passing the sample out of the first separation means into the interface means, separating the sample into fractions with the interface means, and separately passing each fraction through the second separation means.

11. A method of claim 10, which includes providing an electric field across each of the said first separation means and said second separation means with a high voltage power source.

15 12. A method of claim 11, wherein said first separation means is a capillary electrophoresis system and said second separation means is a sieving electrophoresis system.

13. A method of providing high solution separation and high sensitivity detection of components in biological samples, the method comprising:

20 (a) passing a biological sample through a first separation means selected from the group consisting of: isoelectric focusing electrophoresis systems, SDS polyacrylamide gel electrophoresis system, a free solution electrophoresis system, a micellar electrokinetic chromatography system, a reversed phase liquid chromatography system, a normal phase chromatography system, an ion exchange chromatography system, and a size exclusion chromatography system;

25 (b) passing the sample out of the first separation means and separating the sample into fractions;

5 (c) ~~passing each fraction separately through a second separation means selected from the group consisting of: isoelectric focusing electrophoresis systems, SDS polyacrylamide gel electrophoresis system, a free solution electrophoresis system, a micellar electrokinetic chromatography system, a reversed phase liquid chromatography system, a normal phase chromatography system, an ion exchange chromatography system, and a size exclusion chromatography system;~~

10 (d) ~~detecting components of the sample leaving the second separation means with a detector, wherein the method includes applying voltages across said first separation means and said second separation means.~~

14. A method as claimed in claim 13, which includes mixing the sample with a derivatizing agent in the interface means.

15. The method of claim 15, wherein said detector is a high sensitivity laser induced fluorescent detector and wherein the derivatizing agent reacts with components of the sample to make the components fluorescent.

16. The method of claim 15, wherein said first separation means is an isoelectric focusing electrophoresis system, and said second separation means is a sieving electrophoresis system.

17. A method as claimed in any one of claims 10 to 16, the method comprising providing a plurality of first separation means and a plurality of second separation means and a plurality of interface means, with each interface means providing a link between a respective one of the first separation means and respective one of the second separation means, and wherein the method further comprises, for each of the first and second separation means linked by a respective interface means, passing a biological sample through the first separation means to achieve a first

separation, passing the sample out of the first separation means into the respective interface means, separating the sample into fractions with the interface means and separately passing each fraction through a second separation means.

5 18. A method as claimed in claim 17, which comprises providing all the interface means in a common manifold, and providing the manifold with an inlet, for connection to buffer reservoirs, a valve means permitting selective connection to a desired buffer reservoir, a channel network connecting the inlet to the plurality of interface regions, 10 providing each interface region with a port connected to a respective first separation means, a port connected to a respective second separation means and a third, waste port, wherein the method comprises providing a plurality of buffer reservoirs connected to the inlet of a manifold and operating the valve means to connect a selected buffer reservoir to the 15 manifold, whereby the same buffer reservoir is connected to all the interface regions and similar processing steps occur simultaneously in the interface regions.

19. A method as claimed in claim 17 or 18, which further includes providing a planar surface with a plurality of immobilization sites for capturing cells, providing the first separation means with capillary tubes having inlet ends and mounting the inlet ends in an array corresponding to the location of immobilization agents on the planar surface, and wherein the method further comprises providing a biological sample on the planar surface, whereby at least one cell is captured by each immobilization agent site, aligning the inlet ends of the capillary tubes of the first separation means with the immobilization agent sites, and drawing the cells into the capillary tubes of the first separation means, for effecting a first separation in each capillary tube.

20. A method as claimed in claim 19, wherein each

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immobilization site is sized to retain a single cell.

21. A manifold for use in separation and detection of components for the sample, the manifold comprising an inlet, for connection to buffer reservoirs and valve means permitting selective connection to a desired buffer reservoir; a channel network connecting the inlet to a plurality of interface regions; wherein each interface region comprises a port for connection to a first separation means, a port for connection to a second separation means and a third, waste port.

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